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Controversy Surrounds Europe's New Pharma Manufacturing Law

European Union (EU) legislation designed to prevent sub-quality drugs and drug intermediates reaching EU markets is due to come into force at the end of October. The legislation focuses on quality controls at manufacturing plants in Europe and at plants exporting to the region. The rules require any company marketing a certain medicine to source only "starting materials" made under GMP conditions. Materials include active pharmaceutical ingredients (API).

European custom pharma intermediate manufacturers say they hope the new law will curb the flood of sub-quality drugs entering the EU but are concerned that the new law will not be enforced. "About 80% of APIs used in medicines in Europe originate from factories in Asia that have never been inspected," said Guy Villax, CEO of custom pharma intermediates manufacturer Hovione (Lisbon) and a member of the European Fine Chemicals Group (EFCG), in a presentation to an IBC (London) conference at the Chemspec show held recently in Dusseldorf. A plant that is not inspected, even "if it is modern, may not be managed according to a system of continuous improvement," Villax says. "And a wonderful company on the surface may be disposing of [its waste] elsewhere." Cefic recently created EFCG to promote the interest of European fine chemical manufacturers, its activities include trying to halt the flow of sub-quality drugs entering into the EU.

EFCG has been meeting with European politicians in recent months to highlight the issue. "The meetings have been very positive and politicians understand the issue," Villax says. "I don't think they were really aware that 80% of medicines are made from APIs in Asia. I think this probably came as a shock," he says. Companies that are not in compliance with required manufacturing standards "are making much more money as a result," he adds. Leading custom manufacturers in Europe say they hope the legislation will operate in a similar manner to FDA's cGMP, and that under the EU's new legislation companies will be subject to plant inspection audits to meet quality criteria in management systems and performance.

The European Commission is in discussions with the custom manufacturing industry on how to give the new legislation "teeth," Villax says. "We need regulation and we need to take action. If you have guidelines to provide safe quality medicines and don't enforce them, they are not credible. I would like regulators to come forward and say how they are going to enforce them, and what kind of sanctions are going to be put in place. Here in the pharma industry that exists in Europe we continue to do good business essentially because of the U.S. market. We are used to the gold standard of FDA. In the U.S., if you lie or defraud you go to jail—it's very simple. But here in Europe you hardly ever hear of sanctions against non-compliance," he says.

Villax: Among those at ChemSpec concerned about policing of new EU law.

The API Committee (APIC), another Cefic group, also is concerned that the new EU regulation will not be policed effectively. APIC says on its position paper on the issue that it "fears inspections [of plants manufacturing for the EU market] will be fairly limited, considering the limited resources available for such inspections. GMP for APIs can only be enforced if inspection is mandatory and if reinspections take place regularly," APIC adds.

Such inspections are necessary because downward pressure on pricing is leading some EU medicine manufacturers to source more raw materials in Asia, where some manufacturers are able to lower costs because of their sub-standard GMP and regulatory compliance, APIC says. APIC cites various examples of sub-standard medicines reaching the EU market, which it says presents "substantial risks."

Some executives at Europe-based pharma intermediate firms exhibiting at the ChemSpec show say, however, that they are hopeful the new EU legislation will be well enforced and have a significant impact on the market. Imminent introduction of the legislation "is a good sign," says Vincent Touraille, a director at pharma intermediates manufacturer and fine chemical firm PCAS (Longjumeau, France). "We survive against low-cost Chinese competition as long as the competition is fair," Touraille says. "When Chinese and Indian companies deliver the same product as us to the same quality, we can compete. The main problem we have is that certain API products are imported into Europe without any control and from companies that don't comply with any GMP standards. There are companies in Europe that are delighted to import drugs or APIs, change the labels, and sell on to the market. This is now the main fear of companies such as PCAS. We certainly accept competition if it is on the same fair basis," he says.

There is widespread industry concern that the EU's GMP legislation falls far short of the standard set by the FDA. "What is done by the U.S. is not done by Europe," Vincent says. "We want the same to be done in Europe. The new legislation will oblige importers to ensure that the product is manufactured in a responsible manner," he says.

There may be fundamental problems policing the new legislation, however, according to one senior API industry source that chose not to be named. "There is no way [the commission] will have policing in place by November," he says. The commission instead "may be looking to industry to provide an alternative audit system for manufacturing plants that will ensure compliance," the source says.

The key underlying and "unspoken" issue is that EU member governments are content to go along with the status quo because it means a guaranteed supply of low-cost generics, and they will not enforce the new law, the source says. EU member states do not want to pay for top brand APIs and are allowing cheap APIs that may be sub-quality into the market, he adds. National governments may be reluctant to back the policing of stringent API manufacturing plant audits because doing so may increase the cost of some pharmaceutical products, the source adds.

—ALEX SCOTT *in Dusseldorf*